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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/434,105	05/03/1995	DAVID A FISCHHOFF	38-21(13553)	2627

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MONSANTO COMPANY
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ST. LOUIS, MO 63167

EXAMINER

KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
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1638

MAIL DATE	DELIVERY MODE
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05/30/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

08/434,105

Applicant(s)

FISCHHOFF ET AL.

Examiner

Anne R. Kubelik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 3/12/07.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 47-119 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 47-119 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 5/3/95 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I in the reply filed on 12 March 2007 is acknowledged. Applicant's arguments are persuasive, and all Groups are examined.
2. The protest filed by a third party on 5 April 2006 was considered, but not found applicable to the instant claims. The protest was over the now cancelled claim 40, which was drawn to a synthetic gene, and indicates details the restriction filed in the parent between the method of making and the product. As the instant claims are only to the method of making, and the product claims are in the child, Application 10/102,469, protestee's arguments do not apply to the instant case.
3. The instant parent applications, 07/959,506, 07/476,661 and 07/315,355 are currently designated lost by the Office, and thus not available to the Examiner. Examiner's evaluation of the restriction filed in 07/476,661 is based solely on the protest's summary. The Examiner would appreciate Applicant sending a copy of this restriction, and any subsequent papers relevant to it.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. Claims 47-119 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

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art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for the phrase “derived from *Bacillus*” in claims 47, 51, 55, 59, 63, 67, 112, 113, 117 and 119. Nowhere in the specification or the originally filed claims is the starting material a derived sequence.

Neither the instant specification nor the originally filed claims appear to provide support for the concept of the insecticidal protein coding sequence being from any *Bacillus* species. The specification indicates that insecticidal protein coding sequences only from *Bacillus thuringiensis* were considered (see pg 16, lines 28, to pg 22, line 24, and originally filed claims 3, 9, 13, and 30).

Neither the instant specification nor the originally filed claims appear to provide support for the concept of producing a coding sequence that is substantially devoid of polyadenylation signal sequences but not substantially devoid of ATTTA sequences and vice versa. In original claims 13 and 33 the sequences are substantially devoid of both.

Neither the instant specification nor the originally filed claims appear to provide support for the starting material being coding sequences portions of two or more insecticidal polypeptides, as in claims 55 and 67. The only starting sequences originally conceived are an existing structural gene or the wild-type sequence or the starting materials for de novo synthesis (specification, pg 22, lines 24, to pg 23, lines 20, pg 31, lines 25-26; original claims 3, 9, and 30; Fig 1A and B).

Neither the instant specification nor the originally filed claims appear to provide support for the starting material or protein being hybrids of at least any two B.t. insecticidal proteins or their coding sequences, as in claims 91-92.

Neither the instant specification nor the originally filed claims appear to provide support for using coding sequences for an amino-terminal chloroplast transit peptide or a secretion signal sequence, as in claim 108.

Neither the instant specification nor the originally filed claims appear to provide support for the insecticidal protein being an insecticidal fusion, as in claim 114.

Neither the instant specification nor the originally filed claims appear to provide support for “designing a nucleotide sequence” in part (a) of claims 113 and 117.

Neither the instant specification nor the originally filed claims appear to provide support for making any *Bacillus* derived structural genes containing no more than one, seven or two ATTTA and/or Table II polyadenylation sequences or none at all. The specification, in Examples 1 and 4, only describes doing this in specific *Bacillus thuringiensis* sequences, not in any one.

Thus, such a phrases and concepts constitute NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrases and concepts or to cancel the new matter.

6. Claims 47-199 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure that is not enabling. Checking for P-signals and 30 bp long A+T-rich regions, critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Figure 1A and B,

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which describes the method for modification of an existing structural gene (See pg 23, line 17, to pg 24, line 18), requires checking for P-signals and 30 bp long A+T-rich regions.

7. Claims 47-119 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A full review of the specification indicates that *Bacillus thuringiensis* Cry endotoxin coding and amino acid sequences are essential to the operation of the claimed invention. The claims, however, are directed toward use of genus of coding and amino acid sequences for any insecticidal protein from any *Bacillus* species.

The only structures described in the specification are a few *Bacillus thuringiensis* Cry endotoxin coding and amino acid sequences. The specification does not describe the structural features of the full scope of insecticidal proteins from any *Bacillus* species.

Additionally, claims specify that the starting sequence is derived from *B.t. tenebrionus*, but the specification does not describe the structural features of any insecticidal protein from such species.

Lastly, the specification does not describe any starting coding sequences or wild-type *B. thuringiensis* that have an A+T content of about 62%.

Thus, one of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species

Because the sequences are not described, the method of using the sequences to make structural genes is likewise not described, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the compositions used in the claimed methods, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 47-58 and 63-111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

The terms "reduced" and "reducing" in claims 47-58 are relative terms that render the claim indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. What are they reduced relative to?

Claims 63-67, 112 and 117-118 are indefinite in their recitation of "substantially devoid". "substantially" is a relative term, that renders the claim indefinite - what level of reduction is considered "substantial"? For purposes of examination, any level of reduction is considered "substantial".

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 47-70, 81-82, 84-85, 87-88, 93-100, 102-104, 106-107, 109-119 rejected under 35 U.S.C. 103(a) as being unpatentable over Beremand et al (1989, US Patent 4,888,282) in view of Fischhoff et al (1987, Bio/Technol. 5:807-813).

The claims are drawn to methods of making a structural gene using site directed mutagenesis or de novo synthesis of nucleic acids encoding *Bacillus* insecticidal toxins to reduce the number of ATTTA and/or polyadenylation sequences.

Beremand et al disclose that codons of a gene must be matched to that of plants and repeats eliminated, suggested using site-directed mutagenesis and de novo synthesis to make the sequence, and a presented a codon usage table for plants (Table 1, column 6, lines 40-58). Beremand et al also suggest removing the GC doublet whenever possible (column 6, lines 51-54). Beremand et al do not disclose modification of Cry-encoding sequences.

Fischhoff et al teach expressing truncated *Bacillus thuringiensis* endotoxin HD-1 in tomato plants from a construct comprising a plant promoter and polyadenylation sequences (pg 810, left column, paragraphs 2-3).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of codon optimization as taught by Beremand et al, to codin- optimizes the truncated or full-length HD-1 sequence described in Fischhoff et al. One of

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ordinary skill in the art would have been motivated to do so because Fischhoff et al teaches that the level of expression of the HD-1 mRNA was very low (pg 810, left column, paragraph 3), and the unmodified form may be unstable (pg 811, right column, paragraph 1). In modifying two IleTyr codons in HD-1, that starting at base 325 (ATTTAC), and that starting at base 799 (ATTTAT) to ATCTAC using the ILE and Tyr preferred codons in Table I of Beremand et al, one would “substantially” reduce the number of ATTTA sequences and polyadenylation sequences (ATTTAT) in the coding sequence, as well as the number of five consecutive A+T regions in the sequence. The resulting sequence would be more highly expressed in a dicot plant cell, although the amino acid sequence of the protein would not be changed as “sense” codons would be substituted, and would be “substantially devoid” of ATTTA sequences and polyadenylation sequences.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 47-58 and 67-68 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 71-72 of copending Application No. 10/102,469. Although the conflicting claims are not identical, they are not patentably distinct from each other. Methods of making a structural gene using site directed mutagenesis or de novo synthesis of nucleic acids encoding *Bacillus* insecticidal toxins and starting with coding sequence(s) or nucleotide sequence(s) to reduce the number of ATTTA and/or polyadenylation sequences, as claimed in the co-pending application, are species of the genus of the methods of making a structural gene to reduce the number of ATTTA and/or polyadenylation sequences in nucleic acids encoding *Bacillus* insecticidal toxins, as claimed in the instant application; the resultant sequences would be "substantially devoid" of polyadenylation and ATTTA sequences because they would have fewer.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.


Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the

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USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne Kubelik, Ph.D.
May 25, 2007



ANNE KUBELIK, PH.D.
PRIMARY EXAMINER